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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/756,818	01/13/2004	Stephen James Russell	07039-416002	2374
26191	7590	12/20/2005	EXAMINER	
FISH & RICHARDSON P.C. PO BOX 1022 MINNEAPOLIS, MN 55440-1022			LIETO, LOUIS D	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/756,818	Applicant(s) RUSSELL ET AL.	
	Examiner Louis D. Lieto	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 07 November 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 19-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed. ~
- 6) ☒ Claim(s) 19-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/07/05 has been entered.

It is noted that applicant has presented the exact same claim set as was previously examined in the office actions of 8/24/05, 6/03/2005 and 12/01/2004. Further, applicant has not presented any new arguments that differ from those set forth in the reply received on 8/05/2005. Claims 19-26 are pending and under consideration.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method comprising a) transfecting a cell with a nucleic acid sequence encoding a protein operably linked to a tetracycline regulatable promoter *in vitro*, and b) increasing expression of the protein using tetracycline *in vitro*, does not reasonably provide enablement for administering the cells to a mammal that has had an immune response against the protein in order to treat cancer. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to a method of *ex vivo* gene therapy, wherein the disclosed utility is cancer therapy, comprising administering cells that contain a construct encoding an antigen that the subject mammal has previously made an immune response to; wherein antigen expression is controlled by a drug inducible promoter, such as a tet-off promoter.

The claims require increasing expression of a protein in a cell after it has been administered into a mammal, wherein said mammal has had an immune response against said protein prior to administering the cells. The only disclosed purpose for such methods is for therapy (e.g. pg 2, line 12, "cancer therapy"; pg 3, lines 2 1-23, "leukocytes that elicit an anti-tumor effect" pg 8, line 24, "therapeutic (immunogenic) protein"). Further, the specification teaches that the claimed method is intended to produce circulating PBMC T cells that are targeted to and react against tumor cells. However, while the specification teaches construction of a representative vector comprising the tet-off system, transfection of jurkat T cells and expression of the vector in said jurkat T cells in the absence of tetracycline or a tetracycline analog, the specification does not provide any guidance on use of the transfected jurkat T cells in a method of *ex vivo* gene therapy (Example 1). Further, the specification does not provide any guidance on any nucleic acid sequences encoding an immunogenic polypeptide that can be used to treat cancer. Finally, while it is noted that applicants claims encompass any cell, such as a B cell, monocyte, macrophage or any other cell, the specification does not provide an enabling disclosure how these cells are to be used in a method of *ex vivo* cancer therapy in order to produce circulating PBMC T cells that are targeted to and react against tumor cells.

As stated previously, without specific guidance the combination of vector, promoter, level of expression, target tissue, dosage and route of administration required to obtain a therapeutic effect using gene therapy were unpredictable at the time of filing. In Ross et al. (Sept. 10, 1996, Human Gene Therapy, Vol. 7, page 1781-1790) the *ex vivo* approach used to treat tumors resulted in only one melanoma patient **who might be** considered to have had a clinical response, however it may have occurred spontaneously because melanoma is known to regress spontaneously (page 1786, column 1, paragraph 2). Ross et al concludes that it is unpredictable whether a therapeutic result can be obtained using *ex vivo* gene therapy (page 1786, column 1, paragraph 2). Verma et al. (Sept. 18, 1997, Nature, Vol. 389, pages 239-242) states the *in vivo* approach of gene therapy is unpredictable because of an inability to deliver genes efficiently and to obtain sustained expression (see page 239, 3rd column, line 10). "Although more than 200 clinical [gene therapy] trials are currently underway worldwide, with hundreds of patients enrolled, there is still no single outcome that we can point to as a success story" (page 239, column 1, line 16). Thus, the state of the art of gene therapy is such that there is a lack of correlation between expression of a gene product and therapeutic effect using gene therapy methods.

These issues remain as current problems in the field of gene therapy. Pfeifer and Verma state that even "though gene therapy holds great promise for the achievement of this task, the transfer of genetic material into higher organisms still remains an enormous technical challenge {Pfeifer and Verma (2001) Annu. Rev. Genomics. Hum. Genet. 2:177-211; pg. 177, pgph 1}. Johnson-Saliba et al. concurs stating, "although thousands of patients have been involved in clinical trials for gene therapy, using hundreds of different protocols, true success has been

limited. A major limitation of gene therapy approaches, especially when non-viral vectors are used, is the poor efficiency of DNA delivery.” {Johnson-Saliba et al. (2001) Curr. Drug. Targets 2:371-99; Abstract}. Such problems with delivery continue to plague the field of gene therapy. Shoji et al. has characterized the current state of the art as the “tragic failure of gene therapy” because of poor delivery of gene based-medicines due to the lack of an appropriate vector that “fulfills the necessary requirements, including high transfection efficiency, non-toxicity, non-pathogenicity, non-immunogenicity, [and] non-tumorigenicity.” {Shoji et al. (2004) Current Pharmaceutical Design 10 :785-796}. The long-standing problems in the field of gene therapy indicate that the results observed by the applicants by transfecting jurkat T cells *in vitro*, are not sufficient to allow a practitioner skilled in the art to predict how to successfully practice the claimed invention as a method of *ex vivo* gene therapy,

To further support the unpredictability of the combination of elements required to obtain a therapeutic effect using gene therapy, the following references are provided: Miller et al. (1995, FASEB J., Vol. 9, pages 190-199) reviews the types of vectors available for *in vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances in targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain M. (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art, which show

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promise, but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Crystal R.G. (1995, Science, Vol. 270, page 404-410) also reviews various vectors known in the art and indicates that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

The specification demonstrates transfecting Jurkat cells with a vector encoding a chimeric T-cell receptor (scFv-TCR) operably linked to the tet-off operator. The expression of the scFv-TCR is inhibited by increasing the concentration of tetracycline *in vitro* (page 31). Generally, the specification does not provide an enabling disclosure on administering any cells to any mammal, regulating protein expression in a mammal, or obtaining any therapeutic effect in a mammal. Specifically, the specification does not provide an enabling disclosure on how to use cells expressing scFv-TCR *in vivo*, how to increase expression of the scFv-TCR after the cells have been administered to a mammal, or why such cells would be administered to a mammal having an immune response against the scFv-TCR. The specification does not correlate the cells expressing scFv-TCR to cells expressing a protein that could be therapeutic in a mammal that has had an immune response to the protein. Overall, the specification does not overcome the unpredictability in the art by teaching the level of expression, route of administration, vector, promoter or cells required to obtain a therapeutic effect as an *ex vivo* method of cancer therapy. Given the lack of guidance provided in the specification taken with the unpredictability in the art, it would have required one of skill in the art undue experimentation to determine the parameters required to obtain a therapeutic effect using the method claimed.

Further, merely increasing expression of a protein in the absence of therapeutic effect does not have a disclosed use in a mammal having an immune response to the protein prior to administering the cell. The only disclosed purpose for such methods is for therapy (e.g. pg 2, line 12, "cancer therapy"; pg 3, lines 2 1-23, "leukocytes that elicit an anti- tumor effect" pg 8, line 24, "therapeutic (immunogenic) protein"). The specification does not overcome the art established unpredictability of gene therapy by teaching the level of expression, route of administration, vector, promoter or cells required to obtain a therapeutic effect. Pg 16, line 26, through pg 18, line 14 contemplates how to make cells encoding a protein operably linked to a promoter. Additionally, Pg 17, lines 14-29, for example contemplates how to make a lymphocyte transfected with a vector encoding a T-cell receptor operably linked to a regulatable promoter. However, it cannot be determined how to use such a cell for therapy upon being introduced into a host. Pg 10, line 9, thorough pg 16, line 24, describes regulatable promoter systems but does not teach the combination of elements required to treat a patient as a method of cancer therapy. Further, the specification does not enable administering the cell to a mammal and increasing expression of the protein *in vivo*. While the specification does discuss possible drug-regulatable promoters, the only one described in the working examples is the Tet-off promoter. However, the specification does not provide adequate guidance on the use of the Tet-off promoter or any other promoter to regulate protein expression *in vivo* or to determine the combination of elements required to use the method claimed to obtain a therapeutic effect. For example, pg 15, lines 14-21, teaches a vector encoding GM-CSF under the control of a Tet-off promoter; however, the specification does not provide guidance on how to use such a vector for therapy or why one would obtain a mammal having "an immune response against a polypeptide" such as GM-CSF



and administer a vector encoding GM-CSF to such a mammal. The specification does not provide adequate guidance on how to regulate protein expression *in vivo*, or to determine the combination of elements required to use the method claimed, to obtain a therapeutic effect.

Miller et al. (May 1, 1997, Human Gene Therapy, Vol. 8, pages 803-815) teaches the gene regulation system that can be applied to gene therapy in humans is yet unknown (page 809, column 2, line 42). Applicants do not demonstrate regulating any genes in humans or in any art recognized *in vivo* model. Without such guidance, the specification does not enable regulating the expression of a transgene in a mammal as claimed. In particular, the specification does not enable regulating the expression of a polypeptide by “altering the amount of regulatory drug” after the cell has been administered as encompassed by claim 19. The specification does not teach dosage, routes of administration or methods of targeting cells transfected with the polypeptide such that expression can be regulated after the cells have been introduced.

The claims are directed toward various regulatable systems including the tetracycline system. Miller et al. teaches that it is unpredictable which cells the tetracycline system may be applied to (page 809, column 2, 2nd 111 paragraph). Applicants demonstrate transfecting T-cells with a chimeric TCR under the control of a tetracycline system and controlling expression *in vitro* (page 29), but do not correlate the results obtained to other cell lines such that any cell line is enabled. Thus, if applicants intend to claim using the tetracycline regulatory system, the claims should be limited to Jurkat T cells, which are enabled in the specification. Without adequate guidance as to what cells can be used to express proteins using the tetracycline regulatory system, it would require the skilled practitioner undue experimentation to determine which cells can be used with the tetracycline regulatory system.

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Given the lack of guidance in the specification on how to regulate any cells expression of a nucleic acid sequence encoding a immunogenic polypeptide *in vivo*, the lack of guidance on producing any therapeutic affect by administering the cells to any mammal with an immune response to the polypeptide, the art taught unpredictability of obtaining a therapeutic effect using gene therapy, the lack of teachings of any other drug-regulatable promoter for use *in vitro*, a practitioner skilled in the art would be unable to practice the invention as claimed, except as a method comprising a) transfecting a cell with a nucleic acid sequence encoding a protein operably linked to a tetracycline regulatable promoter *in vitro*, and b) increasing expression of the protein using tetracycline *in vitro*, without arduous and extensive experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 19-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is indefinite because the metes and bounds of what the applicants mean by "altering the amount of regulatory drug" in step (c) cannot be determined. The term "altering" encompasses a range of changes from reducing the amount of drug administered to zero or raising it to near toxic levels. Further the specification does not define what the term "altering" means in the context of the various available drug-regulatable promoter systems. Therefore the metes and bounds of the claims cannot be determined. Claims 20-26 depend on claim 19.

*Response to Arguments*

Applicant's arguments filed 11/07/05 have been fully considered but they are not persuasive. It is noted that applicant has not presented any new arguments that differ from those set forth in the reply of 8/05/2005 and addressed in the advisory action of 8/24/05.

Applicant argues that Examiner believes that gene therapy will not be enabled until it is clinically available in humans, and cites *In re Brana* in defense of their position. However, *Brana* can be distinguished from the instant application for several reasons. First the fact pattern is different; *Brana* is drawn to pharmaceutical compounds, while the instant invention is one of gene therapy. Second, the claims in *Brana* are drawn to a compound, while the claims of the instant application are drawn to a method of using nucleic acid sequences in gene therapy. Applicant is incorrect in their conclusion that the examiner believes that gene therapy will only be enabled when it is clinically available in humans. The issue at hand is whether applicant has disclosed sufficient information to enable the claimed method for use in a method of *ex vivo* gene therapy, wherein the intended use is a treatment of cancer. Applicant's specification does not provide sufficient guidance to a skilled practitioner in the art to predict how to practice the invention as claimed.

The requirement for full enablement is that the specification teaches the practitioner in the art how to practice the claimed invention to the full extent of the scope of the claims. As previously noted; applicant has only provided data from in vitro experiments. As stated above and in prior office actions, the disclosed in vitro experiments are insufficient to enable the claimed methods for the stated use of "cancer therapy." The only disclosed purpose for the claimed methods is for gene therapy (e.g. pg 2, line 12, "cancer therapy"; pg 3, lines 2 1-23,

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"leukocytes that elicit an anti- tumor effect" pg 8, line 24, "therapeutic (immunogenic) protein").

As evidenced by the references cited above and in the prior office actions, there is a level of general unpredictability in the art of gene therapy, which requires a detailed disclosure that would allow one skilled in the art to predictably practice the claimed invention.

Applicant argues that the art cited by the examiner fails to support the allegation that gene therapy is so unpredictable that the ordinary practitioner in the art could not practice gene therapy without undue experimentation. Again, the issue is whether the art supports the enablement rejection indicating that the specification fails to disclose how to predictably practice the claimed method of gene therapy without extensive and undue experimentation. It is noted that applicant's working examples were all performed in Jurkat cells *in vivo*. The specification does not provide any guidance on the transfection of autologous primary T cells for use in the claimed invention. Jurkat T cells are a human leukemic cell line with substantially different properties from primary T cells. Specifically, one of the reasons why Jurkat T cells are used for *in vitro* studies is that they are much easier to transfect than primary T cells. At the time of filing "gene transfer into developing and mature primary T cells was limited by the lack of efficient techniques for *ex vivo* or *in vivo* transfection or transduction." {Hurez et al. (2002) BMC Immunology 3:1-14}. Even retroviral transfection had severe limitations which required the construction of specialized transgenic mice in order to produce efficient retroviral transfection of primary mouse T cells (Abstract; pg. 1, col.2-pg. 2col. 2). Applicant's claims encompass a broad range of mammalian subjects beyond these specialized mice. The specification fails to disclose any methods of transfecting primary cells, such as human T cells for use in the claimed invention. Further, at the time of filing neither the art of record nor the specification provided

guidance on the transfection of primary T cells for use in the claimed method of *ex vivo* therapy. Therefore, a skilled practitioner in the art would not be able to predict the efficiency of transfection, or resulting gene expression levels in primary T cells based on the disclosed specification.

Applicant further argues that when examiner addressed the specific subject matter of the presently claimed invention it was stated that the two steps recited in the present claims “may not require undue experimentation.” The implication is that examiner was acknowledging that the method as claimed was enabled. This would be an incorrect reading of the prior rejection and contrary to the examiner’s intended meaning. Applicant’s two steps are to wit: first transfecting cells, which in general is a technique well known in the art. However, for specific cells, most importantly primary cells, this technique is not enabled based on the knowledge level in the art, Therefore the specification disclose sufficient information in order to practice the claimed method. Second, the introduction of cells into a mammal is also enabled as a general technique. However, in applicant’s claimed method of *ex vivo* gene therapy, these two steps are but two building blocks of a series of extensive requirements necessary for the practice of the claimed method of cancer therapy.

Case law teaches (Ex parte Forman, 230 USPQ 546,547 (BPAI 1986)) that “the disclosure of a patent application must enable practice of the invention claimed without undue experimentation”, wherein factors involved in the determination of undue experimentation were deemed to include “the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability

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of the art and the breadth of the claims.” The quantity and complexity of experimentation necessary to practice the claimed invention, as a method of cancer therapy requires that the skilled practitioner determine for himself the combination of specific nucleic acid encoded immunogenic polypeptide, vector, promoter, level of expression, cell to be transfected, target tissue, dosage, route of administration, method of transfection and cancer to be treated in order to obtain a therapeutic effect using the claimed method of *ex vivo* gene therapy. “Case law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not to find out how to use it for themselves.” In re Gardner 166 USPQ 138 (CCPA) 1970. Given the breadth of the claimed invention, the numerous references in the art in regards to the on-going unpredictability in the field of gene therapy, the utter lack of support in the specification for the using the claimed invention as a method of *ex vivo* gene therapy to treat cancer, the rejection of claims 19-26 under 35 U.S.C 112, first paragraph for lack of full scope of enablement is maintained for reasons of record as stated above and in the office actions of 8/24/05, 6/03/2005 and 12/01/2004.

The rejection of original or amended claims 19-26 under 35 U.S.C 112, second paragraph for being indefinite is maintained for reasons of record stated in the office actions of 8/24/05, 6/03/2005 and 12/01/2004. Applicant's arguments filed on 8/05/2005 have been fully considered but they are not persuasive.

Applicant does not raise any new arguments in their response. The term altering in the context of claim one is equivalent to an open ended numerical range that encompasses any change in the amount of regulatory drug to which said cell is exposed. As such the term is

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indefinite. Further, drug-inducible promoters can act to increase or inhibit expression, therefore it is unclear how a promoter, such as the tet-off promoter can increase gene expression from an initial absence of any drug, since the addition of any amount of tetracycline or doxycycline will only decrease expression. Applicant's phrasing is ambiguous to the point that the metes and bounds of the claimed invention cannot be determined.

No claims Allowed.

### *Conclusion*

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

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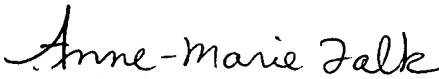
will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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